

Amendments to the Specification:

Please replace the paragraph beginning at page 1, line 4, with the following rewritten paragraph:

The present invention relates to a process of asymmetric alkynylation of ketone or ketimine, particularly, involving the enantioselective addition of terminal alkynes to a trifluoromethyl ketone or ketimine intermediate to give a chiral tertiary proparglic alcohols or amines. The adduct compounds are the key precursors to the potent HIV reverse transcriptase inhibitor Efavirenz (DMP 266), DPC 961₂ and DPC 083. The present invention also relates to the new novel amino alcohol ligand used in the above process.

Please replace the paragraph beginning at page 1, line 11, with the following rewritten paragraph:

Human immunodeficiency virus (HIV) is prone to mutation, which leads to drug resistance. It is known that some compounds are reverse transcriptase inhibitors and ~~are~~ effective agents in the treatment of HIV[,] and similar diseases, e.g., azidothymidine or AZT. DPC083, DPC 961₂, and Efavirenz (Sustiva TM) are second generation HIV non-nucleoside reverse transcriptase inhibitors (NNRTIs) with enhanced potency. Efavirenz (Sustiva TM) has been approved for the treatment of HIV (Antimicrob. Agents Chemother. 1995, 39, 2602). DPC083 and DPC 961 are under currently-undergoing clinical evaluation (Journal of Medicinal Chemistry vol.43, no.10, 2000, 2019-2030). Please replace the paragraph beginning at page 1, line 19, with the following rewritten

paragraph:

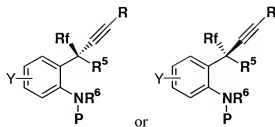
Some methods have been reported for the synthesis of Efavirenz (Sustiva TM) (Angew. Chem. Int. Ed. no. 5, 1999, 711-713; Journal of Organic Chemistry vol.63, no. 23, 1998, 8536-8543), DPC083, and DPC 961. These prior methods disclose the preparation of prepared DPC 961 by a fractional crystallization or 1,4-diastereoselective addition protocol[], both employing an auxiliary (Journal of Organic Chemistry vol.68, no.3, 2003, 754-761; Tetrahedron Letter vol.41, 2000, 3015-3019). Very recently, WO0170707 discloses ~~disclosed~~ an asymmetric process for preparing DPC961 via chiral ligand mediated asymmetric addition. However, in the ~~this~~ process, a large amount of excess strong base (lithium alkyl and LHMDs) and excess chiral ligand have been ~~was~~ used under very strict condition (-20°C).

Please replace the subtitle beginning at page 2, line 1, with the following rewritten paragraph:

Disclosure Summary of the Invention invention

Please replace the paragraph beginning at page 2, line 19, with the following rewritten paragraph:

In this invention, ~~there is disclosed a~~ The process of the present invention which uses an amino alcohol ligand as a catalyst for the asymmetric synthesis of the chiral compound of the structure

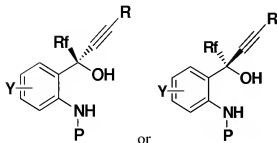


where Y is H, mono- or multi-substituted electron-withdrawing group or electron-donating group, ~~preferred is preferably~~, H, mono- or di-substituted electron-withdrawing group or electron-donating group, wherein Y can be located at *m*-, *o*-, or *p*-position of the benzene ring[;] More preferably, Y is H, Cl, Br, CH₃SO₂, CH₃CH₂SO₂, NO₂, or F. Most preferably, Y is F, Cl, Br[;] P is hydrogen or an amino protecting group[;],

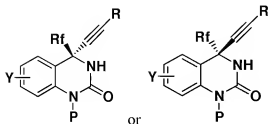
Rf is ~~a~~ fluoro-containing alkyl, ~~preferred is preferably~~, a C₁~C₂₀ fluoro-containing alkyl, ~~and more preferably, a preferred is~~ C₁~C₄ fluoro-containing alkyl[;],

R is ~~a~~ trialkylsilyl, alkyl, cycloalkyl or aryl group[;],

R⁶ is hydrogen when R⁵ is hydroxy[.] of the structure:



Also, R^5 and R^6 can be cyclization such as -HNCO- of the structure



where Y, P, R, Rf is the same as above.

Please replace the paragraph beginning at page 3, line 20, with the following rewritten paragraph:

The process comprises ~~Comprising~~ the steps of:

Please replace the paragraph beginning at page 4, line 9, with the following rewritten paragraph:

In an a preferred embodiment, ~~quenehing~~ the above reaction is quenched by adding a proton source[,] to give the desired compound. ~~Preferable~~ Preferably, the proton source is a saturated aqueous solution of NH₄Cl aqueous (sat.), water, aqueous hydrochloric acid or citric acid ~~aqueous~~.

Please replace the paragraph beginning at page 9, line 26, with the following rewritten paragraph:

~~In this invention, there is also disclosed~~ The present invention provides a novel chiral ligand ~~of the structure~~ or its enantiomer having the structure as follows:

Please replace the paragraph beginning at page 15, line 3, with the following rewritten paragraph:

The present invention provides ~~provided~~ a novel ligand. The use of the ligand relates to asymmetric addition, particularly, ~~to~~ a direct synthesis of the optically active DPC 961, DPC083, and efavirenz[,] by chiral addition of zinc or copper acetylide to a ketimine intermediate to give a propargylic amine, with enantiomeric excess up to 99%[,], or by chiral addition of zinc or copper acetylide to an ketone intermediate to give a propargylic alcohol.

Please replace the paragraph beginning at page 15, line 8, with the following rewritten paragraph:

Compared with the prior methods of preparation DPC 961, the process of the present this invention provides ~~achieved with~~ a chiral amino alcohol to mediate the addition reaction along an asymmetric pathway. The previous prior methods of by-a derivatization and fractional crystallization or 1, 4-diastereoselective addition protocol[,] both employ an ~~employing~~ auxiliary(*Journal of Organic Chemistry* vol.68, no.3, **2003**, 754-761; *Tetrahedron Letter* vol.41, **2000**, 3015-3019). WO 200170707 discloses ~~disclosed a~~ an asymmetric process ~~processes~~ for preparing DPC961 via chiral moderated asymmetric addition. However, ~~in this~~ the process uses a large amount of excess strong

base (lithium alkyl and LHMDs) and excess chiral ligand ~~was used~~ under very strict condition (-20°C), while the process of ~~this~~ the present invention can be performed with very mild reaction condition ($20-40^{\circ}\text{C}$). The ligand used in the reaction of the present invention is less expensive.[.] ~~further more it~~ Furthermore, the ligand in the reaction of the present invention can be recycled. The workup is also very simple. All of the advantages render the reduction of this will reduced the cost of the process greatly.

Please replace the subtitle beginning at page 16, line 7, with the following rewritten paragraph:

Detailed Description of Best Mode for Carrying Out the Invention